

## **AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

### **Listing of claims:**

- 1-18. (canceled)
19. (previously presented) An immune adjuvant composition comprising
- (a) a saponin possessing immune adjuvant activity, wherein the saponin is derived from *Quillaja saponaria*; and
- (b) an immunostimulatory oligonucleotide comprising at least one unmethylated CpG dinucleotide,
- wherein the immunostimulatory oligonucleotide is not a part of a DNA vaccine vector.
20. (canceled)
21. (previously presented) The immune adjuvant composition as claimed in claim 19, wherein the saponin comprises a substantially pure saponin.
22. (previously presented) The immune adjuvant composition as claimed in claim 21, wherein the substantially pure saponin comprises QS-7, QS-17, QS-18, or QS-21.
23. (previously presented) The immune adjuvant composition as claimed in claim 22, wherein the substantially pure saponin comprises QS-21.
24. (currently amended) The immune adjuvant composition as claimed in claim 19, wherein the immunostimulatory oligonucleotide comprises ~~a CpG motif comprising~~ more than one unmethylated CpG dinucleotide.
25. (currently amended) The immune adjuvant composition as claimed in claim 19, wherein the immunostimulatory oligonucleotide comprises one or more chemical groups phosphate-modified nucleotides selected from the group consisting of phosphorothioate, alkylphosphonate, phosphorodithioate, alkylphosphorothioate, phosphoramidate, 2-O-methyl, carbamate, acetamidate, carboxymethyl ester, carbonate, and phosphate triester.
26. (currently amended) The immune adjuvant composition as claimed in claim ~~25~~ 19, wherein ~~at least one of the one or more phosphate-modified nucleotides the~~

immunostimulatory oligonucleotide comprises at least one is-a phosphorothioate modified nucleotide.

27. (previously presented) The immune adjuvant composition as claimed in claim 19, wherein the immunostimulatory oligonucleotide comprises a CpG motif having the formula 5' $X_1$ CG $X_2$ 3', wherein  $X_1$  is adenine, guanine, or thymine, and  $X_2$  is cytosine, thymine, or adenine.

28. (currently amended) The immune adjuvant composition as claimed in claim ~~27~~ 19, wherein the ~~CpG motif~~ immunostimulatory oligonucleotide comprises TCTCCCAGCGTGCGCCAT (SEQ ID NO:1).

29-62. (canceled)

63. (previously presented) An immune adjuvant composition comprising  
(a) a saponin possessing immune adjuvant activity, wherein the saponin is derived from *Quillaja saponaria*; and  
(b) an immunostimulatory oligonucleotide comprising at least one unmethylated CpG dinucleotide,  
wherein the saponin comprises substantially pure QS-7, QS-17 or QS-18.

64. (currently amended) A method for inducing ~~the~~ an immune response in an individual to an antigen comprising (1) administering to the individual an amount of the immune adjuvant composition as claimed in claim 63 effective to induce the immune response~~[[,]]; and (2) administering to the individual wherein said individual is administered a nucleic acid molecule comprising a nucleotide sequence encoding the antigen, wherein the nucleic acid molecule is administered separately from the immune adjuvant composition or in the same formulation with the immune adjuvant composition; and wherein (1) and (2) induce an immune response in the individual to the antigen.~~

65. (currently amended) An immune adjuvant composition comprising  
(a) a saponin possessing immune adjuvant activity, wherein the saponin is derived from *Quillaja saponaria*; and  
(b) an immunostimulatory oligonucleotide comprising at least one unmethylated CpG dinucleotide,  
wherein the immunostimulatory oligonucleotide comprises one or more chemical groups ~~phosphate-modified nucleotides~~ selected from the group consisting of phosphorothioate, alkylphosphonate, phophorodithioate, alkylphosphorothioate,

phosphoramidate, 2-O-methyl, carbamate, acetamidate, carboxymethyl ester, carbonate, and phosphate triester.

66. (currently amended) The immune adjuvant composition as claimed in claim 65, wherein the immunostimulatory oligonucleotide comprises at least one of the one or more phosphate-modified nucleotides is a phosphorothioate modified nucleotide.

67. (currently amended) A method for inducing ~~the~~ an immune response in an individual to an antigen comprising (1) administering to the individual an amount of ~~an~~ the immune adjuvant composition as claimed in claim 65 ~~effective to induce the immune response~~[[,]]; and (2) administering to the individual wherein said individual is administered a nucleic acid molecule comprising a nucleotide sequence encoding the antigen, wherein the nucleic acid molecule is administered separately from the immune adjuvant composition or in the same formulation with the immune adjuvant composition; and wherein (1) and (2) induce an immune response in the individual to the antigen.

68. (currently amended) A method for inducing ~~the~~ an immune response in an individual to an antigen comprising (1) administering to the individual an amount of the immune adjuvant composition as claimed in claim 66 ~~effective to induce the immune response~~[[,]]; and (2) administering to the individual wherein said individual is administered a nucleic acid molecule comprising a nucleotide sequence encoding the antigen, wherein the nucleic acid molecule is administered separately from the immune adjuvant composition or in the same formulation with the immune adjuvant composition; and wherein (1) and (2) induce an immune response in the individual to the antigen.

69. (previously presented) An immune adjuvant composition comprising  
(a) a saponin possessing immune adjuvant activity, wherein the saponin is derived from *Quillaja saponaria*; and  
(b) an immunostimulatory oligonucleotide comprising at least one unmethylated CpG dinucleotide,

wherein the immunostimulatory oligonucleotide comprises  
TCTCCCAGCGTGCGCCAT (SEQ ID NO:1).

70. (currently amended) A method for inducing ~~the~~ an immune response in an individual to an antigen comprising (1) administering to the individual an amount of the immune adjuvant composition as claimed in claim 69 ~~effective to induce the immune response~~[[,]]; and (2) administering to the individual wherein said individual is

~~administered~~ a nucleic acid molecule comprising a nucleotide sequence encoding the antigen, wherein the nucleic acid molecule is administered separately from the immune adjuvant composition or in the same formulation with the immune adjuvant composition; and wherein (1) and (2) induce an immune response in the individual to the antigen.

71. (previously presented) An immune adjuvant composition comprising  
(a) a saponin possessing immune adjuvant activity, wherein the saponin is derived from *Quillaja saponaria*; and  
(b) an immunostimulatory oligonucleotide comprising at least one unmethylated CpG dinucleotide,  
wherein the immunostimulatory oligonucleotide comprises  
TCCATGACGTTCTGACGTT (SEQ ID NO:2).

72. (currently amended) A method for inducing ~~the~~ an immune response in an individual to an antigen comprising (1) administering to the individual an amount of the immune adjuvant composition as claimed in claim 71 ~~effective to induce the immune response~~[[,]]; and (2) administering to the individual ~~wherein said individual is administered a nucleic acid molecule comprising a nucleotide sequence encoding the antigen, wherein the nucleic acid molecule is administered separately from the immune adjuvant composition or in the same formulation with the immune adjuvant composition;~~ and wherein (1) and (2) induce an immune response in the individual to the antigen.

73. (previously presented) An immune adjuvant composition comprising  
(a) a saponin possessing immune adjuvant activity, wherein the saponin is derived from *Quillaja saponaria*; and  
(b) an immunostimulatory oligonucleotide comprising at least one unmethylated CpG dinucleotide, wherein the immunostimulatory oligonucleotide is 4-40 bases in length.

74. (currently amended) A method for inducing ~~the~~ an immune response in an individual to an antigen comprising (1) administering to the individual an amount of the immune adjuvant composition as claimed in claim 73 ~~effective to induce the immune response~~[[,]]; and (2) administering to the individual ~~wherein said individual is administered a nucleic acid molecule comprising a nucleotide sequence encoding the antigen, wherein the nucleic acid molecule is administered separately from the immune adjuvant composition or in the same formulation with the immune adjuvant composition;~~ and wherein (1) and (2) induce an immune response in the individual to the antigen.



75. (previously presented) An immune adjuvant composition comprising

(a) a saponin possessing immune adjuvant activity, wherein the saponin (i) is derived from *Quillaja saponaria* and (ii) is a chemically modified saponin; and

(b) an immunostimulatory oligonucleotide comprising at least one unmethylated CpG dinucleotide.

76. (currently amended) A method for inducing ~~the~~ an immune response in an individual to an antigen comprising (1) administering to the individual an amount of the immune adjuvant composition as claimed in claim 75 effective to induce the immune response[[,]]; and (2) administering to the individual wherein said individual is administered a nucleic acid molecule comprising a nucleotide sequence encoding the antigen, wherein the nucleic acid molecule is administered separately from the immune adjuvant composition or in the same formulation with the immune adjuvant composition; and wherein (1) and (2) induce an immune response in the individual to the antigen.

77. (previously presented) The composition of claim 19, wherein the saponin is a chemically modified saponin.

78. (currently amended) The immune adjuvant composition as claimed in claim ~~27~~ 19, wherein the immunostimulatory oligonucleotide comprises ~~a CpG motif comprising~~ TCCATGACGTTCTGACGTT (SEQ ID NO:2).

79-89. (canceled)

90. (currently amended) A method for inducing ~~the~~ an immune response in an individual to an antigen comprising (1) administering to the individual an amount of the immune adjuvant composition as claimed in claim 19 effective to induce the immune response[[,]]; and (2) administering to the individual wherein said individual is administered a nucleic acid molecule comprising a nucleotide sequence encoding the antigen, wherein the nucleic acid molecule is administered separately from the immune adjuvant composition or in the same formulation with the immune adjuvant composition; and wherein (1) and (2) induce an immune response in the individual to the antigen.

91. (canceled)

92. (currently amended) The method as claimed in any of claims claim 64, 67, 68, 70, 72, 74, 76, or 90, wherein the saponin comprises a substantially pure saponin.

93. (previously presented) The method as claimed in claim 92, wherein the substantially pure saponin comprises QS-7, QS-17, QS-18, or QS-21.

94. (previously presented) The method as claimed in claim 93, wherein the substantially pure saponin comprises QS-21.

95. (currently amended) The method as claimed in any of claims claim 64, 67, 68, 70, 72, 74, 76, or 90, wherein the immunostimulatory oligonucleotide comprises ~~a CpG motif comprising~~ more than one unmethylated CpG dinucleotide.

96. (currently amended) The method as claimed in any of claims claim 64, 70, 72, 74, 76, or 90, wherein the immunostimulatory oligonucleotide comprises one or more chemical groups phosphate-modified nucleotides selected from the group consisting of phosphorothioate, alkylphosphonate, phosphorodithioate, alkylphosphorothioate, phosphoramidate, 2-O-methyl, carbamate, acetamidate, carboxymethyl ester, carbonate, and phosphate triester.

97. (currently amended) The method as claimed in any of claims claim 64, 70, 72, 74, 76, or 90 ~~96~~, wherein ~~at least one of the one or more phosphate-modified nucleotides is a~~ the immunostimulatory oligonucleotide comprises at least one phosphorothioate modified nucleotide.

98. (currently amended) The method as claimed in any of claims claim 64, 67, 68, 70, 72, 74, 76, or 90, wherein the immunostimulatory oligonucleotide comprises a CpG motif having the formula 5' $X_1$ CG $X_2$ 3', wherein  $X_1$  is adenine, guanine, or thymine, and  $X_2$  is cytosine, thymine, or adenine.

99. (currently amended) The method as claimed in any of claims claim 64, 67, 68, 74, 76, or 90 ~~98~~, wherein the immunostimulatory oligonucleotide ~~comprising a CpG motif comprising~~ comprises TCTCCCAGCGTGCGCCAT (SEQ ID NO:1) or TCCATGACGTTCTGACGTT (SEQ ID NO:2).

100. (currently amended) The method as claimed in any of claims claim 64, 67, 68, 70, 72, 74, 76, or 90, wherein the individual is an animal.

101. (previously presented) The method as claimed in claim 100, wherein the animal is a mammal.

102. (currently amended) The method as claimed in any of claims claim 64, 67, 68, 70, 72, 74, 76, or 90 ~~101~~, wherein the individual is a human.

103. (currently amended) An ~~immune-adjuvant~~ vaccine composition comprising  
(a) a saponin possessing immune adjuvant activity, wherein the saponin is derived from *Quillaja saponaria*;

(b) an immunostimulatory oligonucleotide comprising at least one unmethylated CpG dinucleotide; and

(c) a nucleic acid molecule comprising a nucleotide sequence encoding an antigen, wherein the nucleotide sequence is operatively linked to a promoter,

wherein the immunostimulatory oligonucleotide is not a part of the nucleic acid molecule comprising the nucleotide sequence encoding the antigen.

104. (canceled)

105. (currently amended) The ~~immune-adjuvant~~ vaccine composition as claimed in claim 103, wherein the saponin comprises a substantially pure saponin.

106. (currently amended) The ~~immune-adjuvant~~ vaccine composition as claimed in claim 105, wherein the substantially pure saponin comprises QS-7, QS-17, QS-18, or QS-21.

107. (currently amended) The ~~immune-adjuvant~~ vaccine composition as claimed in claim 106, wherein the substantially pure saponin comprises QS-21.

108. (currently amended) The ~~immune-adjuvant~~ vaccine composition as claimed in claim 103, wherein the immunostimulatory oligonucleotide comprises a ~~CpG-motif~~ comprising more than one unmethylated CpG dinucleotide.

109. (currently amended) The ~~immune-adjuvant~~ vaccine composition as claimed in claim 103, wherein the immunostimulatory oligonucleotide comprises one or more chemical groups phosphate-modified-nucleotides selected from the group consisting of phosphorothioate, alkylphosphonate, phosphorodithioate, alkylphosphorothioate, phosphoramidate, 2-O-methyl, carbamate, acetamidate, carboxymethyl ester, carbonate, and phosphate triester.

110. (currently amended) The ~~immune-adjuvant~~ vaccine composition as claimed in claim ~~109~~ 103, wherein ~~at least one of the one or more phosphate-modified-nucleotides is a~~ the immunostimulatory oligonucleotide comprises at least one phosphorothioate modified nucleotide.

111. (currently amended) The ~~immune adjuvant~~ vaccine composition as claimed in claim 103, wherein the immunostimulatory oligonucleotide comprises a CpG motif having the formula 5'X<sub>1</sub>CGX<sub>2</sub>3', wherein X<sub>1</sub> is adenine, guanine, or thymine, and X<sub>2</sub> is cytosine, thymine, or adenine.

112. (currently amended) The ~~immune adjuvant~~ vaccine composition as claimed in claim ~~111~~ 103, wherein the immunostimulatory oligonucleotide comprises ~~a CpG motif comprising~~ TCTCCCAGCGTGCGCCAT (SEQ ID NO:1) or TCCATGACGTTCTGACGTT (SEQ ID NO:2).

113. (currently amended) The method of any of claims 64, ~~67, 68~~, 70, 72, ~~74~~, 76, or 90, wherein the nucleic acid molecule comprising a nucleotide sequence encoding the antigen is administered to the individual within 2 days of said administering of the immune adjuvant composition.

114. (previously presented) The method of claim 113, wherein the nucleic acid molecule encoding the antigen is administered to the individual concurrently with the immune adjuvant composition.

115-116. (canceled)

117. (previously presented) An adjuvant composition comprising a QS21 and an immunostimulatory oligonucleotide containing an unmethylated CpG dinucleotide.

118. (previously presented) An adjuvant composition according to claim 117 further comprising a carrier.

119. (previously presented) An adjuvant composition as claimed in claim 117, wherein said immunostimulatory oligonucleotide comprises a CpG motif having the formula 5'X<sub>1</sub>CGX<sub>2</sub>3', wherein X<sub>1</sub> is adenine, guanine, or thymine, and X<sub>2</sub> is cytosine, thymine, or adenine.

120. (previously presented) An adjuvant composition as claimed in claim 117, wherein said immunostimulatory oligonucleotide is selected from the group comprising: TCCATGACGTTCTGACGTT (SEQ ID NO:1) and TCTCCCAGCGTGCGCCAT (SEQ ID NO:2).

121. (previously presented) An adjuvant composition as claimed in claim 118, wherein said carrier is selected from the group comprising a capsule, liquid solution,



suspension or elixir for oral administration, or a sterile liquid such as a solution or suspension.

122. (previously presented) An immunogenic composition comprising an adjuvant composition as claimed in claim 117 or 118, further comprising an antigen.

123. (previously presented) An immunogenic composition as claimed in claim 122, wherein said antigen is derived from an organism selected from the group comprising: Human Immunodeficiency Virus, Hepatitis B virus, Influenza virus, Mycobacteria, or Plasmodium.

124. (previously presented) An immunogenic composition as claimed in claim 122 wherein the vaccine is administered systemically.

125. (previously presented) An immunogenic composition as claimed in claim 122 wherein the vaccine is administered mucosally.

126. (previously presented) An adjuvant composition according to claim 117 or 118, wherein QS21 is in the form of a capsule, liquid solution, suspension or elixir for oral administration, or a sterile liquid such as a solution or suspension.

127. (new) The method of any of claims 67, 68, or 74, wherein the nucleic acid molecule comprising a nucleotide sequence encoding the antigen is administered to the individual within 2 days of said administering of the immune adjuvant composition.

128. (new) The method of claim 127, wherein the nucleic acid molecule encoding the antigen is administered to the individual concurrently with the immune adjuvant composition.

129. (new) An adjuvant composition comprising a saponin and an immunostimulatory oligonucleotide.

130. (new) An adjuvant composition according to claim 129 further comprising a carrier.

131. (new) An adjuvant composition as claimed in claim 129 or 130, wherein said saponin is selected from the group comprising Quil A, or purified saponins such as QS21, QS7, or QS17.

132. (new) An adjuvant composition as claimed in any one of claims 129 to 131, wherein said immunostimulatory oligonucleotide comprises a CpG motif having the

formula 5'X<sub>1</sub>CGX<sub>2</sub>3', wherein X<sub>1</sub> is adenine, guanine, or thymine, and X<sub>2</sub> is cytosine, thymine, or adenine.

133. (new) An adjuvant composition as claimed in claims 129 to 132, wherein said immunostimulatory oligonucleotide is selected from the group comprising: TCC ATG ACG TTC CTG ACG TT (SEQ ID NO: 2); TCT CCC AGC GTG CGC CAT (SEQ ID NO: 1).

134. (new) An adjuvant composition as claimed in any one of claims 130 to 133, wherein said carrier is selected from the group comprising a capsule, liquid solution, suspension or elixir for oral administration, or a sterile liquid such as a solution or suspension.

135. (new) A vaccine composition comprising an adjuvant composition as claimed in any one of claims 129 to 134, further comprising an antigen.

136. (new) A vaccine composition as claimed in claim 135, wherein said antigen is derived from an organism selected from the group comprising: Human Immunodeficiency Virus, Hepatitis B virus, Influenza virus, Mycobacteria, or Plasmodium.

137. (new) A vaccine composition as claimed in claims 135 to 136 wherein the vaccine is administered systemically.

138. (new) A vaccine composition as claimed in claims 135 to 136 wherein the vaccine is administered mucosally.

139. (new) A method of inducing an immune response in an individual, comprising the systemic administration of an effective amount of the vaccine composition as claimed in claims 135 to 136.

140. (new) A method of treatment of an individual susceptible to a disease by the administration to an individual of an effective amount of the vaccine as claimed in any one of claims 135-138.

141. (new) A method of treatment as claimed in claim 140, wherein the administration of the vaccine is through a systemic route.

142. (new) A vaccine as claimed in claim 135 for use as a medicament.

143. (new) Use of a combination of a saponin and a CpG molecule in the manufacture of a vaccine for the prophylaxis of viral, bacterial, or parasitic infections.

144. (new) Use of a combination of a saponin, an immunostimulatory oligonucleotide and a carrier in the manufacture of a vaccine for the prophylaxis of viral, bacterial, or parasitic infections.

145. (new) A method of inducing a systemic antigen specific immune response in a mammal, comprising administering to a mucosal surface of said mammal a composition comprising an antigen and a saponin and a CpG molecule.

146. (new) Method of making an adjuvant composition comprising admixing a saponin with an immunostimulatory oligonucleotide.

147. (new) Method of making an adjuvant composition comprising admixing a saponin, an immunostimulatory oligonucleotide, and a carrier.

148. (new) Method of making a vaccine comprising admixing the following (a) a saponin, (b) an immunostimulatory oligonucleotide, and (c) an antigen.

149. (new) Method of making a vaccine comprising admixing the following (a) a saponin, (b) an immunostimulatory oligonucleotide, (c) a carrier and (d) an antigen.